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Epigenetic-based hormesis and age-dependent altruism: Additions to the behavioural constellation of deprivation

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Abstract: We support Pepper and Nettle's (P&N's) hypothesised adaptive responses to deprivation. However, we argue that adaptive responses to stress shift with age. Specifically, present-oriented behaviours are adaptive for young people (e.g., in terms of mating and reproduction) but costly for older people in deprived communities who would benefit from investing in grandchildren. Epigenetic mechanisms may be responsible for age-related tactical shifts.

Pepper & Nettle (P&N) have delivered an important contribution to the field by hypothesising that people exhibit behaviourally adaptive responses to deprivation. Further, we are pleased that the authors acknowledge that DNA methylation may play a role in the behavioural constellation of deprivation (BCD). Caution is needed, as most human behavioural epigenetics research (among healthy individuals) is correlational or blood- or saliva-based and therefore does not permit an understanding of the underlying functional molecular physiology. Inflammation is only one logical possibility, as suggested by P&N, but epigenetic profiles involved in the BCD likely vary by age and tissue type. For example, DNA methylation, a well-studied epigenetic alteration, varies by age, sex, tissue, cell type, and isoform, making blood-based correlational studies potentially misleading. Work by Horvath (2013) on the epigenetic clock indicates that, regardless of tissue type, chronical age can be predicted with high accuracy from DNA methylation profiles. In the case of pathological tissue (e.g., cancerous tumours), epigenetic age is advanced relative to healthy tissue (Horvath 2013; 2015). We argue that

the precision of the epigenetic clock indicates specific life-history adaptations that are system-wide. In the case of impoverished environments, we suspect from an evolutionary and epigenetic perspective that adaptive responses to stress by young people (e.g., present-oriented behaviours) should be qualitatively distinct from the adaptive responses to stress by older people (e.g., future-oriented behaviours, such as altruism and giving social support). Indeed, we hypothesise that if older people were to maintain a BCD strategy suggested by P&N, they would be at an inclusive fitness disadvantage compared to those who employ a life-history-dependent shift (e.g., caring for grandchildren, community-based altruism). From an epigenetic-profiling perspective, we expect a shift in profiles as we age to correlate with changes in the behavioural adaptive responses to deprivation. For example, the behavioural strategy that works best for a 21-year-old facing deprivation would be costly for a 60-year-old. There is an important analogy to be made between the emphasis on mating for younger people and the shift toward parenting among older people. Brown (2015) suggests that genes important for growth (e.g., development of secondary sexual characteristics, such as big muscles in young men) could become costly later in life (e.g., development of cancers). Such effects are consistent with antagonistic pleiotropy perspectives on senescence, the proposal by Williams (1957) that a gene controlling one trait could be beneficial to the organism's fitness at younger ages and detrimental to the organism's fitness later in life. We believe it is important for P&N to extend the BCD model to incorporate epigenetic adaptive responses to antagonistic pleiotropy, which may be more marked in deprived environments.

A second related issue raised by P&N is the importance of studying pathological responses to deprivation. Specifically, they propose in the target article abstract that they "emphasise the idea that the present-oriented behaviours of the constellation are a contextually appropriate response to structural and ecological factors rather than a pathology." Experimental work on the epigenetics of stress in humans and other organisms suggests an inverted U or J relation between stress and adaptive responses (Bernal et al. 2013; Park et al. 2017). This nonlinear relation between stress and adaptive responses can be called a "hormesis effect" (Chalk & Brown 2014). In the case of

deprivation and epigenetics, evidence suggests that early exposure to extreme stress changes our epigenome in ways that place us at increased risk of disease. Swartz et al. (2017) show how DNA methylation is related to risk-linked amygdala activity, which would be adaptive in harsh environments, a finding that is consistent with P&N. However, at extreme levels, these epigenetic changes may lead to depression or possibly suicide, which would likely be maladaptive, especially among older people, where community-based altruism may be beneficial to health in impoverished or low SES communities (Brown et al. 2005; Martinez et al. 2006).

In conclusion, present-oriented behaviours are adaptive in younger people for reproduction purposes; however, from an inclusive fitness perspective, grandparental investment is beneficial at older ages. This may help explain why even in older, deprived communities, altruism is positively correlated with health (Brown et al. 2005). Extreme present-oriented selfish behaviours may be strongly selected against among older individuals in deprived communities due to inclusive fitness losses or the costs of competing against younger individuals. Finally, experimental work on epigenetics in rodents (Bernal et al. 2013; Waterland & Jirtle 2003) clearly shows that *high* levels of stress *in utero* cause negative outcomes, whilst *moderate* levels of stress are beneficial. We do believe that a molecular epigenetic approach provides a useful extension to P&N's BCD approach. Age-dependent BCD can be tested using measures of developmental disruption at the molecular epigenetic (DNA methylation dysregulation as a barometer of stress, e.g., Horvath 2013; Park et al. 2017; Waterland & Jirtle 2003) and behavioural levels of analysis (e.g., prolonged sociopathy in older people). Manifestations of present-oriented behaviours in older people from deprived communities would be an example of pathology. In contrast, future-oriented altruism and giving social support (e.g., community volunteerism, especially among older people in impoverished communities; Brown et al. 2005) are expected to be more viable condition-dependent strategies relative to present-oriented behaviours.

References [William Michael Brown and Rose Jyoti Olding **[WMB]**

Bernal, A. J., Dolinoy, D. C., Huang, D., Skaar, D. A., Weinhouse, C. & Jirtle, R. L. (2013) Adaptive radiation-induced epigenetic alterations mitigated by antioxidants. *FASEB Journal* 27(2):665–71. [WMB]

Brown, W. M. (2015) Exercise-associated DNA methylation change in skeletal muscle and the importance of imprinted genes: A bioinformatics meta-analysis. *British Journal of Sports Medicine* 49(24):1567–78. [WMB]

Brown, W. M., Consedine, N. S. & Magai, C. (2005) Altruism relates to health in an ethnically diverse sample of older adults. *Journals of Gerontology* 60B(3):143–52. [WMB]

Chalk, T. E. W. & Brown, W. M. (2014) Exercise epigenetics and the fetal origins of disease. *Epigenomics* 6(5):469–72. [WMB]

Horvath S. (2013) DNA methylation age of human tissues and cell types. *Genome Biology* 14(10):R115. [WMB]

Horvath, S. (2015) Erratum to: DNA methylation age of human tissues and cell types. *Genome Biology* 16:96. [WMB]

Martinez, I. L., Frick, K., Glass, T. A., Carlson, M., Tanner, E., Ricks, M. & Fried, L. P. (2006) Engaging older adults in high impact volunteering that enhances health: Recruitment and retention in The Experience Corps Baltimore. *Journal of Urban Health* 83(5):941–53. [WMB]

Park, S. S., Skaar, D. A., Jirtle, R. L. & Hoyo, C. (2017) Epigenetics, obesity and early-life cadmium or lead exposure. *Epigenomics* 9(1):57–75. [WMB]

Swartz, J. R., Hariri, A. R. & Williamson, D. E. (2017) An epigenetic mechanism links socioeconomic status to changes in depression-related brain function in high-risk adolescents. *Molecular Psychiatry* 22(2):209–14. [WMB]

Waterland, R. A. & Jirtle, R. L. (2003) Transposable elements: Targets for early nutritional effects on epigenetic gene regulation. *Molecular and Cellular Biology* 23(15):5293–300. [WMB]

Williams, G. C. (1957) Pleiotropy, natural selection, and the evolution of senescence. *Evolution* 11(4):398–411. [WMB]